The Influence of hydrodynamic environment on the nucleation mechanism of a chiral crystallization

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Introduction

Crystallization is an important purification and separation technique in the chemical and pharmaceutical industries. Despite a vast number of theories in the literature, the fundamental science behind crystal nucleation and growth is not well understood and operator experience rather than sound scientific understanding plays a major role in the success of a crystallization process. Scaling up from a batch laboratory to an industrial scale process is typically a non-linear operation and is often marred with batch to batch variation and other problems not encountered at the laboratory scale. Recent research into the use of novel oscillatory baffled crystallizer (OBC) technology has shown step change improvements over traditional stirred tank crystallizer (STC) techniques as well as some interesting phenomenon such as seeding is not essential in an OBC whereas it is crucial for an equivalent process in a STC. It is therefore the objective of this thesis work to provide some scientific insight into the comparison of nucleation mechanisms of a seeded crystallization in both the STC and OBC.

Hypothesis

Different fluid dynamic systems in each type of crystallizer (Figure 1) could result in changes in nucleation mechanism.

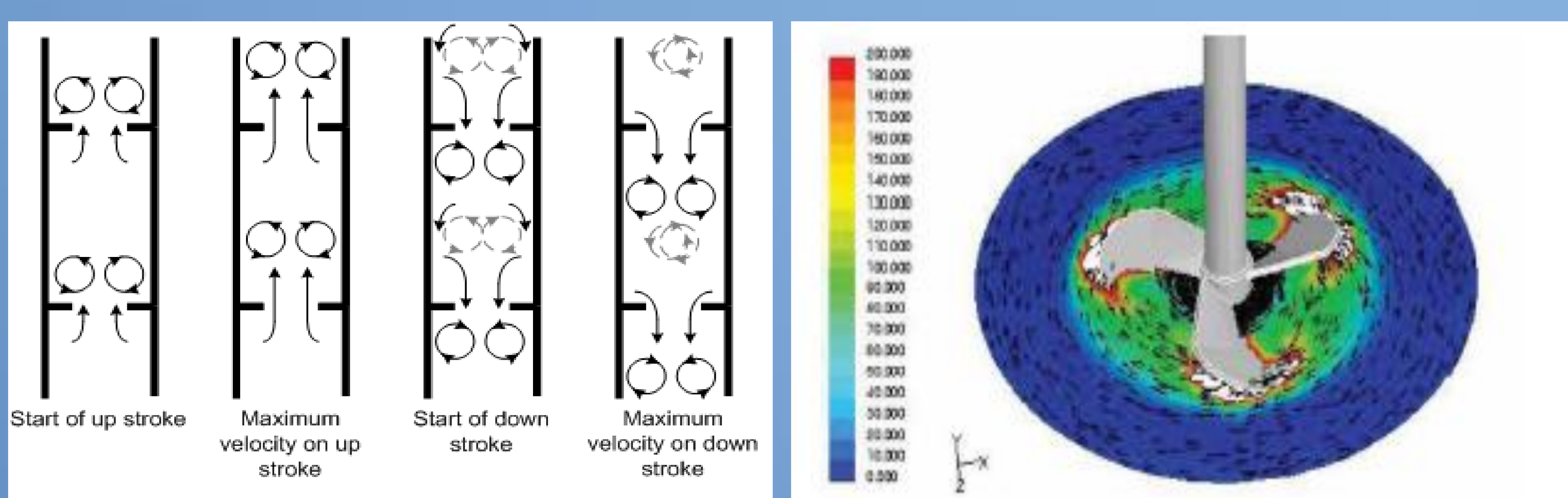

Figure 1 – Uniform vortex mixing in OBC[1] (left) and ineffective mixing in STC[2] (right)

Strategy

•Maintain a constant set of process conditions.
•Vary only the fluid dynamics.
•Use a compound which allows insight into nucleation mechanism.

Model Compound

•Sodium chlorate used in previous studies [3,4].
•A-chiral substance which yields left or right handed crystals.
•Enantiomorphic crystals are optically active (Figure 2).
•The handedness could be related to nucleation mechanism.

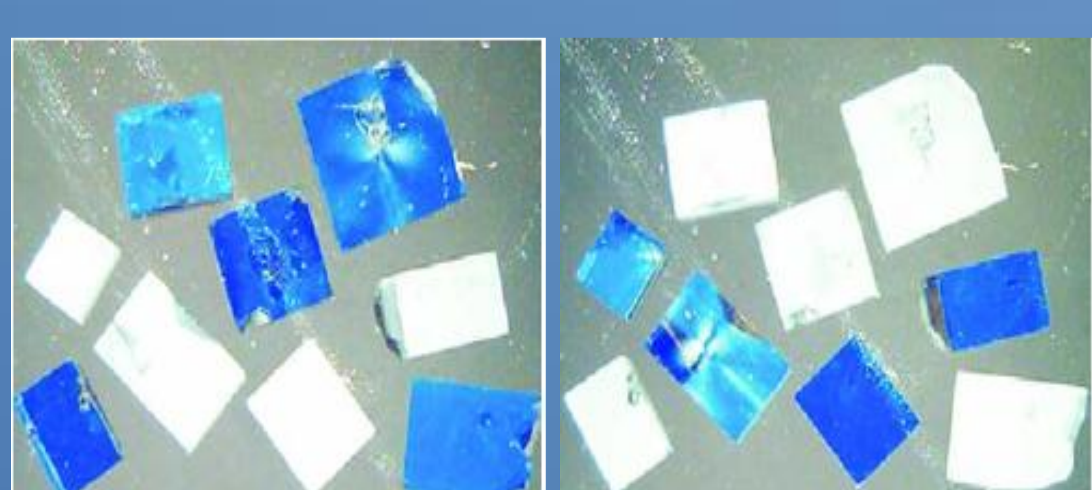

Figure 2 –Polarized light reveals the handedness of product crystals [5]

Experimental setup

•OBC with moving baffles and STC set up according to Figure 3.
•All process conditions the same for both vessels (Tables 1 and 2).

Table 1 – Process conditions

Saturation Temperature (°C)	Wt. $NaClO_3$/100 mL saturated solution (g)	Volume (mL)	Dissolution Temp (°C)	Dissolution time (min)	Supercooling (°C)	Seeding time (min)	Number of repeats
31	73.79	500	40	60	1	3	3

Table 2 – Mixing conditions

Mixing conditions	N_S(RPM)	f(Hz)	x_0(mm)	P/V (W m^{-3})
STC	57	--	--	11.17
OBC	--	0.4	32	11.13

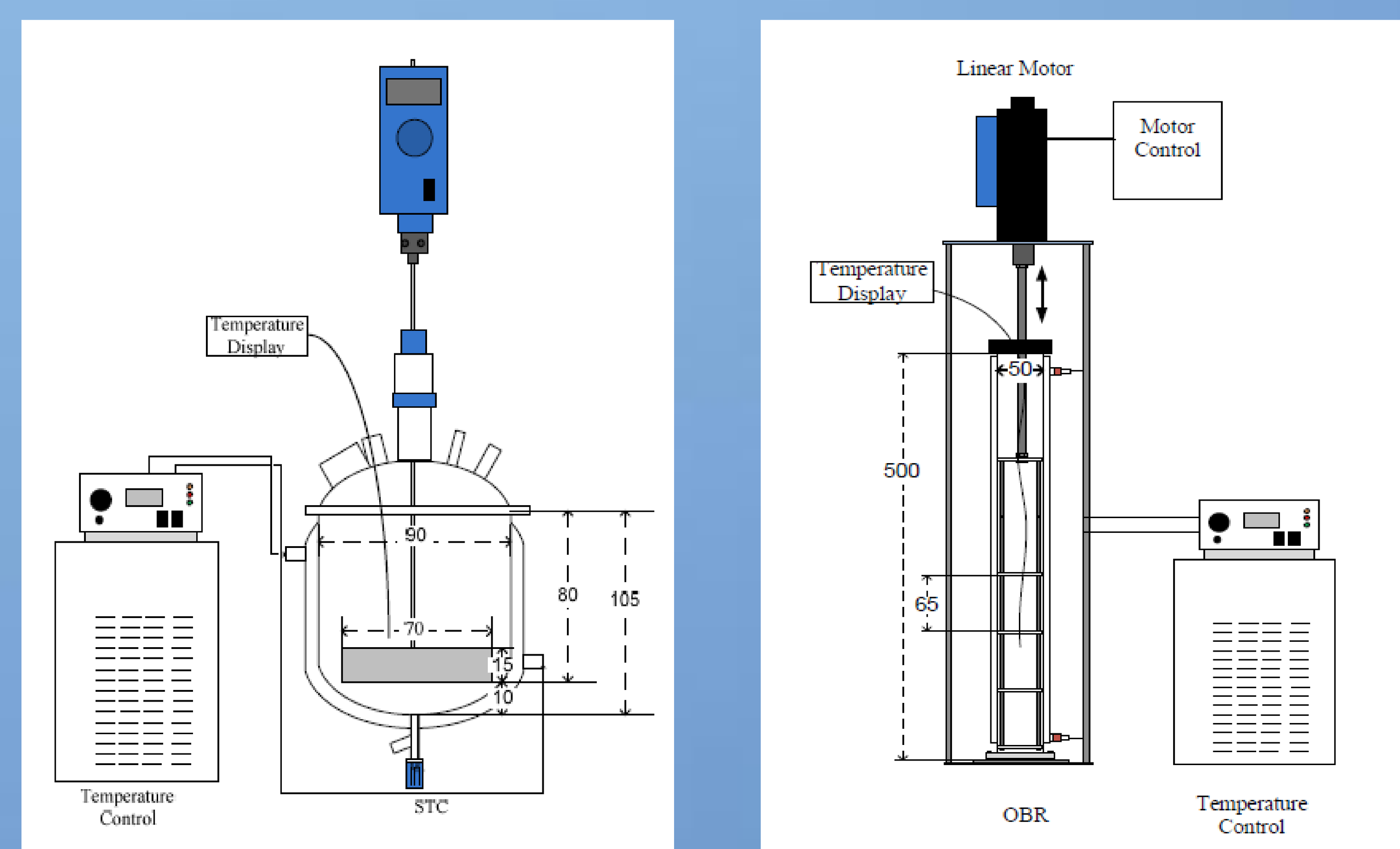

Figure 3 – Schematic setup of the STC (left) and OBC (right) – not to scale

Results

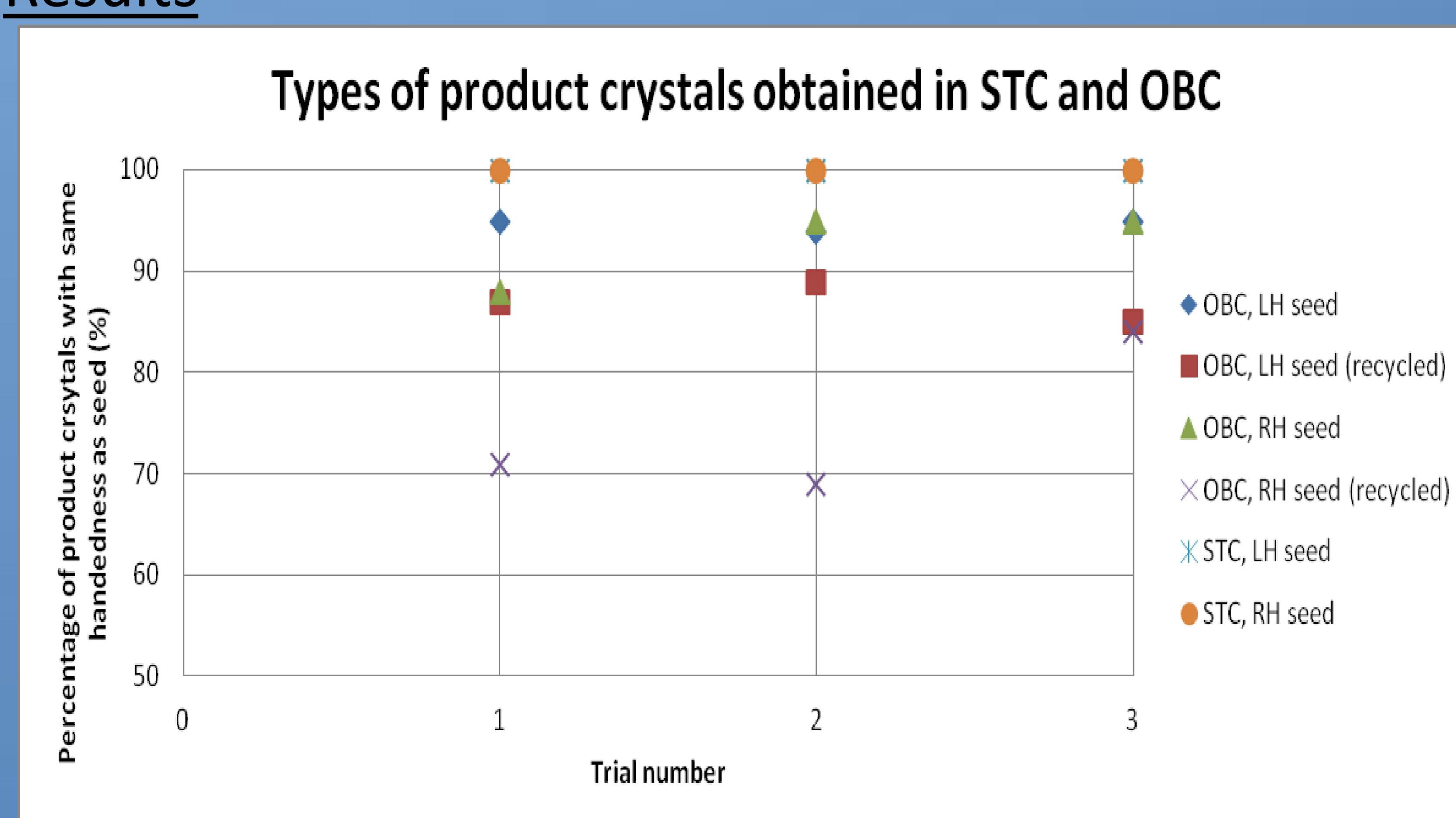

Figure 4 – Types of product crystals obtained in these trials

•STC always yields product crystals with 100 % similarity to seed.
•In OBC this value was always less than or equal to 95 %.
•No mixing yields products with 100 % similarity to seeds.
•STC appears to be dominated by secondary nucleation.
•OBC must have some combination of primary and secondary nucleation.

Causes of difference

•Fluid shear well known to influence nucleation[2,6,7].
•Purity of starting material.
•Microcrystalline dust?

Future research

•Alter the methods of oscillation and stirring.
•Vary the mixing intensity.
•Study various supersaturations.

References

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